

**REMARKS**

Claims 1, 18, 20 and 21 are pending in the application. Claim 20 is rejected. Claims 19 and 20 are objected to. Claims 1, 18 and 21 are allowed.

**A. Claim Rejections - under 35 USC 112**

Claim 20 remains rejected under 35 USC 112, first paragraph, as failing to comply with the written description requirement because the specification does not enable one skilled in the art to treat dysmenorrhea and retinal neuropathy. The Examiner acknowledges Applicants' arguments, but finds them unpersuasive. The Examiner states that the journal articles cited in support of "retinal neuropathy" (Nippon Ganka Gakki Zasshi) showing the activity of EP<sub>2</sub> to depress intraocular pressure and protection of the nerve are directed to a different class of compounds, as is US publication 2005/0124577. The Examiner also states that the data provided by Applicant showing the EP<sub>2</sub> binding activity of compounds within the present invention cannot be found in the US publication. Finally, the Examiner states that Applicant's arguments focus on retinal neuropathy but not on dysmenorrhea.

For the following reasons, the rejection is overcome and/or traversed, respectfully.

Claim 20 has been amended to delete recitation of dysmenorrhea.

Further, as evidence that EP<sub>2</sub> agonists are considered useful to treat retinal neuropathy, such as glaucoma, the Examiner's attention is again directed to the three references submitted previously.

As pointed out in the response to the previous Office action, Nippon Ganka Gakki Zasshi. 1993 March; 97(3):289-96 (Reference 3), J. Ocul. Pharmacol. Ther. 1995 Fall; 11(3):447-54 (Reference 4), and US 5,877,211 (Reference 5), all demonstrate activity of EP<sub>2</sub> to depress intraocular pressure and protect the nerve. This is strong evidence that the presently claimed compounds, which are EP<sub>2</sub> agonists, are useful to treat retinal neuropathy.

Additionally, Applicant previously pointed out that paragraph 0424 in US publication 2005/0124577 shows that the compounds of the present application (for example, the compound described in Example 4(1)) have EP<sub>2</sub> binding activity. Also, because the compound described in Example 4(1) is not included within the scope of the present claims, Applicant submitted data on EP<sub>2</sub> binding activity of compounds within the present claims.

Now, Applicant submits this data on EP<sub>2</sub> binding activity in the form of a Rule 132 Declaration of Tsutomu Shiroya. The declaration explains that CHO cells that express prostanoid receptor sub-types murine EP<sub>1</sub>, EP<sub>2</sub>, EP<sub>3α</sub> and EP<sub>4</sub> were prepared and used as membrane authentic samples. The prepared membrane fractions were incubated with <sup>3</sup>H-PGE<sub>2</sub>, and the amount of bound complex was measured. The K<sub>d</sub> value was obtained from Scatchard plots. Measurement of the binding inhibition for <sup>3</sup>H-PGE<sub>2</sub> with compounds of the present invention was performed by adding <sup>3</sup>H-PGE<sub>2</sub> and the compound of the present invention at a series of concentrations. K<sub>i</sub> of each compound was calculated and the results are shown in the table in the declaration, which is reproduced below.

EP<sub>2</sub> binding activity

Example No.	Ki(nM)
	EP2
6(32)	0.5
6(48)	3.5
6(53)	1.0
6(60)	0.4
6(63)	0.4
6(74)	1.5
6(77)	0.4
6(89)	0.6

From the data in the table, it can be seen that the compounds of the present application are effective for treatment of retinal neuropathy since 1) EP<sub>2</sub> agonists are effective for treatment of retinal neuropathy and ii) the compounds of the present application have EP<sub>2</sub> agonist activity.

Accordingly, the Examiner is requested, respectfully, to reconsider and remove this rejection.

**B. Claim objections**

Claim 19 is objected to as a substantial duplicate of Claim 18. The Examiner asserts that the intended use is not a limitation of a compound. *In re Hack*, 114 PQ 161 (CCPA 1957).

Furthermore, amended Claim 20 is objected to because the word “or” is missing between dysmenorrheal and retinal.

The objections have been addressed by canceling claim 19 and by amending claim 20 to delete recitation of dysmenorrheal.

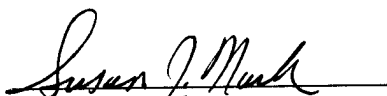
In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the

AMENDMENT UNDER 37 C.F.R. § 1.114(c)  
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Respectfully submitted,

  
Susan J. Mack  
Registration No. 30,951

SUGHRUE MION, PLLC  
Telephone: (202) 293-7060  
Facsimile: (202) 293-7860

WASHINGTON DC SUGHRUE/265550

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